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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/500,700	02/09/00	BARBAS III	C SCRIP1160-4

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Lisa A Haile Ph D
Gray Cary Ware & Friedenrich LLP
4365 Executive Drive Suite 1600
San Diego CA 92121-2189

EXAMINER	
LEFFERS JR,G	
ART UNIT	**PAPER NUMBER**
1636	6

DATE MAILED: 12/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/500,700	Barbas, et al.
Examiner	**Group Art Unit**
Gerald G. Leffers Jr.	1636

☒ Responsive to communication(s) filed on *May 22, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *2-41* is/are pending in the application.

Of the above, claim(s) *6-15, 20-39, and 41* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *2-5, 16-19, and 40* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

SUPPLEMENTAL OFFICE ACTION

This is a Supplemental Office Action mailed in response to the preliminary amendment filed by applicants on 5/22/00, in which claim 1 was canceled and new claims 2-41 were added.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences were set forth that lack sequence identifiers, no CRF was filed, no paper sequence was filed for those sequences and no attorney statement was filed for those sequences. These sequences include sequences listed throughout the specification (e.g. the zinc finger-nucleotide binding motif and amino acid sequence TGEKP given on page 51, lines 16-24) and the sequences given in many of the figures (e.g. Figures 1 and 2). If the Sequence Listing required for the instant application is identical to that of another application, and covers the sequences specified above, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 2422.02).

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. *Any* response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R.

1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

Election/Restriction

I. Claims 2-5, 16-19, and 40, drawn to zinc finger-nucleotide binding polypeptide variants, classified in class 530, subclass 350.

II. Claims 6-7, 20-25, drawn to nucleic acids encoding various zinc finger-nucleotide binding polypeptide variants, classified in class 536, subclass 23.1.

III. Claims 8-15 and 26, drawn to in vitro methods for inhibiting a transcriptional function of a target cellular nucleotide sequence, classified in class 514, subclass 2.

IV. Claims 27-39 and 41, drawn to methods of isolating a zinc finger-nucleotide binding polypeptide variant, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

The proteins of Group I and the nucleic acids of Group II are chemically, biologically, structurally, and functionally distinct from each other and thus one does not render the other obvious. The protein of Group I is not required to produce the DNA of Group II (the DNA can be replicated in vectors without the use of the protein) and the DNA of Group II is not required to

produce the protein of Group II (which can be produced synthetically or isolated from cells). Therefore, the inventions of Groups I-II are capable of supporting separate patents.

Inventions of Group I and Group III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptides of Group I can be used to generate antibodies against the polypeptides.

Inventions of Group I and Groups IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the polypeptides of Group I can be made synthetically or isolated from cells.

Inventions of Groups II and III are biologically and functionally different and distinct from each other and thus one does not render the other obvious. The nucleic acids of Group II are not used in the methods of Group III. The operation, function and effects of the nucleic acids of Group II (i.e. encoding zinc finger-nucleotide binding polypeptide variants) are completely different and distinct from the operation, function and effects of the methods of Group III (i.e. inhibition of a transcriptional function of a target cellular nucleotide sequence). Therefore, the inventions of these different, distinct groups are capable of supporting separate patents.

Inventions of Group II and Group IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of Group II can be used as probes to identify other nucleic acids encoding zinc finger-nucleotide polypeptide proteins from nucleic acid libraries.

The inventions of Groups III and IV are biologically and functionally different and distinct from each other and thus one does not render the other obvious. The methods of Groups III and IV comprise steps which are not present in or required for the methods of the other group: contacting a zinc finger-binding polypeptide variant with a nucleotide sequence motif with an amount of variant effective to inhibit a transcriptional activity of the motif (Group III) and measurement of a reporter gene product encoded by a sequence operably linked to a zinc finger-nucleotide binding motif (Group IV). The end results of the methods are different: inhibition of a transcriptional activity of a nucleotide sequence motif (Group III) and the identification of a nucleotide sequence encoding a zinc finger-binding polypeptide variant (Group IV). Thus, the operation, function and effects of these different methods are different and distinct from each other. Therefore, the inventions of these different, distinct groups are capable of supporting separate patents.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Lisa Haile on 6/1/00 a provisional election was made with traverse to prosecute the invention of Group I, claims 2-5, 16-19 and 40. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6-15, 20-39 and 41 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-5, 16-19 and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 21-22 and 53 of U.S. Patent No. 6,140,466. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

Both sets of claims specify an isolated zinc finger-nucleotide binding polypeptide variant comprising a specified number of zinc finger modules that bind to a cellular nucleotide sequence and modulate the function of the cellular nucleotide sequence. The two sets of claims differ only in the number of zinc finger modules comprised within the variant polypeptide structure and the number of such fingers which must comprise a modification in the amino acid sequence. The cited claims from the '466 patent are drawn towards a zinc finger-binding polypeptide variant

comprising at least three zinc finger modules and further comprising at least one amino acid modification within each of at least three such modules which binds a target cellular nucleotide sequence. The instant claims are drawn towards a zinc finger-binding polypeptide variant comprising at least two (claims 2-5, 18-19 and 40), three (claim 16) or five (claim 17) zinc finger modules wherein at least one of the modules has at least one amino acid sequence modification. Thus, the claims of the '466 patent are entirely encompassed by claims 2-5, 16, 18-19 and 40 of the instant application. Claim 17 of the instant application is merely an obvious variant of the cited claims from the '466 patent. Thus, the instant claims, if allowed, would extend patent protection of the zinc finger-nucleotide binding polypeptide variants of the '466 patent, in addition to providing patent protection to the zinc finger-nucleotide binding polypeptide variants not encompassed by the '466 patent (e.g. variants comprising only two zinc finger modules). Also, if a patent resulting from the instant claims was issued and transferred to an assignee different from the assignee holding the '466 patent, then two different assignees would hold a patent to the claimed polypeptide variants of the '466 patent. Thus, improperly, there would be possible harassment by multiple assignees.

Claims 2-5, 16-19 and 40 are also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 09/500,691. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims specify an isolated zinc finger-nucleotide

binding polypeptide variant comprising a specified number of zinc finger modules that bind to a cellular nucleotide sequence and modulate the function of the cellular nucleotide sequence. The instant claims differ from claim 1 of Application No. 09/500,691 in specifying that at least one of the zinc finger modules has a modification. Claim 1 of Application No. 09/500,691 specifies at least 2 zinc finger modules and the instant claims specify at least 2, 3 and 5 such modules (claims 2, 16 and 17, respectively) and/or the number of nucleotides bound by the zinc finger-binding polypeptide variant (claims 18-19). The instant claims are thus narrower in scope, but totally encompassed by claim 1 of Application No. 09/500,691. The inventions of the instant claims are obvious variants of the invention of Application No. 09/500,691 because it is and was known in the art that the number of modules which interact with the target nucleotide sequence can affect the specificity of the protein/nucleic acid interactions and that one of skill in the art can modify the number and nature of the zinc finger modules in order to affect binding activity. One would have been motivated to construct zinc finger-nucleotide binding protein variants having at least 2, 3 or 5 zinc finger modules which interact with a target nucleotide sequence in order to achieve the expected benefit of altering the specificity with which the polypeptide variants bind target nucleic acid sequences. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specific limitations of "at least three zinc finger modules" and "at least five zinc finger modules" (claims 16-17) do not have support in the specification and, thus, constitute NEW MATTER.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is vague and indefinite in that the metes and bounds of the term "derived from" are unclear. The term is unclear in that the number and nature of steps required to generate a "derivative" of a zinc finger polypeptide are not clearly defined. Would a zinc finger-binding

polypeptide having only the cysteine and histidine residues in common with another zinc finger-binding polypeptide be considered a "derivative" of the other polypeptide? It would be remedial to amend the claim language to clearly indicate what is intended by the term "derived from".

Claim 40 is vague and indefinite in that it is dependent on a nonelected claim. It would be remedial to amend the claim language to incorporate the limitations of claim 27, upon which claim 40 is dependent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 2-5, 16-19 and 40 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hanas et al (U; see the entire document).

Hanas et al teach the construction and isolation of mutants of TFIIIA which either lack the fourth zinc finger of TFIIIA (page 9862; Figure 1A) or comprise a fusion of the 7th and 8th zinc fingers of the protein (page 9862; Figure 1B). Hanas et al further teach that both of the mutants retain the ability to bind their cognate binding sequence and influence transcription of a 5S RNA gene in Xenopus unfertilized egg extracts (Abstract; page 9866; Figures 4 and 5).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 4 and 16-17 rejected under 35 U.S.C. 103(a) as being unpatentable over Crozatier et al (V).

Crozatier et al teach the isolation of four mutants in the serendipity δ (*sry δ*) zinc finger protein of Drosophila. Crozatier et al teach that three of the four mutations in *sry δ* (*sry* δ^{12}, *sry* δ^{SF1} and *sry* δ^{SF2}) are localized to the third zinc finger module (out of seven) of the protein (Abstract; page 914, column 1). That polypeptides of these proteins retain some ability to bind

DNA and affect its function is evident from the teaching of Crozatier at all that the mutants can complement one another (Table 1; page 915, column 1) and that the mutations apparently affect the transcription of different sets of genes at different stages of development (page 915, column 1, paragraph 2). Crozatier et al teach that in vitro experiments to determine the consequences of the *sry* δ^{+}, *sry* δ^{SF1} and *sry* δ^{SF2} mutations on the ability of the encoded polypeptide to specifically bind DNA were in progress at the time of publication (page 915, column 1, paragraph 1).

Crozatier et al do not specifically teach the isolation of the mutant proteins.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to express and purify the polypeptides encoded by the *sry* δ^{SF1} and *sry* δ^{SF2} genes because Crozatier et al teach that such isolation of the mutant proteins was possible at the time the invention was made and because recombinant techniques are and were well known in the art for producing and isolating desired DNA-binding polypeptides. One would have been motivated to do so in order to achieve the expected benefit of performing in vitro analysis of the DNA-binding properties of the mutant proteins relative to the wild type protein, as suggested by Crozatier et al. Absent any evidence to the contrary, there would have been a reasonable expectation of success in isolating the mutant *sry* δ^{SF1} and *sry* δ^{SF2} encoded polypeptides described by Crozatier et al for in vitro analysis of their DNA-binding properties.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Leffers, Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott, can be reached on (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

GLJ

G. Leffers, Jr.

Patent Examiner

Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER

November 21, 2000